

REMARKS

A. Support for Process Claims 37 to 45 and Dimer Claims 46 to 54

Support for making a protected epicatechin-(4 α , 8)-catechin dimer as well as the unprotected dimer may be found in original Claim 6 ". . . wherein the 4-aryl substituent is a derivative of epicatechin or of catechin". See also original Claim 7 ". . . wherein the epicatechin or catechin is linked through the C-8 position of the epicatechin or catechin". Further, see the discussion at page 8, 2nd full paragraph which reads: "In one aspect, the invention relates to a process for the preparation of epicatechin-epicatechin dimers or epicatechin-catechin dimers where the nucleophilic aryl organometallic reagent is derived from a protected 8-bromoepicatechin or a protected 8-bromocatechin or derivative thereof."

Protection of the C-3 hydroxyl of 5, 7, 3', 4'-tetra-O-benzyl-epicatechin with a benzyl group or with a silyl group is discussed at pages 9 and 10. Example 1 shows the preparation of 3, 5, 7, 3', 4'-penta-O-benzyl-epicatechin. Example 7 shows the preparation of 5, 7, 3', 4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-epicatechin. Similar protection of the C-3 hydroxyl of 5, 7, 3', 4'-tetra-O-benzyl-8-bromo-epicatechin or - catechin is discussed at page 10.

Support for oxidizing the C-4 position of the penta-O-protected epicatechin to form the 4-hydroxy group may be found in Examples 2 and 8.

Support for oxidizing the 4-hydroxy group of the protected epicatechin to the 4-ketone may be found in Examples 3 and 9.

Treatment of protected 8-bromo-epicatechin or - catechin with *tert*-butyllithium to form the nucleophilic reagent is discussed at page 10, last paragraph. Preparation of a protected 8-

bromo epicatechin-lithium reagent (not the claimed catechin lithium reagent) and coupling of the lithium reagent with 3, 5, 7, 3', 4' penta-O-protected 4-ketone-epicatechin is exemplified in Examples 10 and 11. Please note that Example 17 shows how to make penta-O-benzyl-8-bromo-catechin which can then be reacted with *tert*-butyllithium (using the procedure carried out in Example 11) with 5, 7, 3', 4'-tetra-O-benzyl-8-bromo-3-O-*tert*-butyldimethylsilyl)-epicatechin and in Example 18 with 3, 5, 7, 3', 4'-penta-O-benzyl-8-bromo-epicatechin.

Reduction of the C-4 hydroxyl group on the penta-O-protected epicatechin-(4 α , 8)-penta-O-protected epicatechin dimer (not the penta-O-protected epicatechin-(4 α , 8)-penta-O-protected catechin dimer) is exemplified in Examples 12 and 19.

Removal of the silyl protecting group from the C-3 position of the penta-O-protected dimer is discussed at page 12, 2nd full paragraph and shown in Example 13. Removal of the benzyl protecting groups from the epicatechin-(4 α , 8)-epicatechin dimer (not the epicatechin-(4 α , 8)-catechin dimer) is discussed at pages 12-13 and shown in Example 20.

Support for acylating the C-3 hydroxyl group to form a derivatized dimer can be found at page 8, lines 1-3 which read ". . . optionally deprotecting the C-3 hydroxyl group and then further optionally acylating the C-3 hydroxyl group with a suitable acylating agent and subsequently removing the benzyl groups". See also Example 14 where the *tera*-O-protected epicatechin-(4 α , 8)-epicatechin dimer (not the tetra-O-protected epicatechin-(4 α , 8)-catechin dimer) was derivatized at the C-3 position of the second mer with 3, 4, 5-tri-O-benzylgalloyl groups and Example 15 where the benzyl protecting groups were removed from the galloyl groups.

Comparable process claims where both monomers in the dimer are epicatechin can be found in U.S. 6, 476, 241. Comparable dimer claims where both monomers are epicatechin can be found in U.S. 6,720,432.

B. Closing

Entry of this Amendment is respectfully requested. No new matter is presented.

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Respectfully submitted,

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